CPCH9861388

Patent Office of the People's Republic of China

Address : Receiving Section of the Chinese Patent Office, No. 6 Tucheng Road West, Haidian District, Beijing.Postal code: 100088

Applicant	AJINOMOTO CO., INC.			**Seal of Examiner**	**Date of Issue**
Agent	China Patent Agent (H.K.) Ltd.				January 10, 2003
Patent Application No.	98103375.X	**Application Date**	July 3, 1998	**Exam Dept.**	
Title of Invention	PROCESS FOR PRODUCING MICROBIAL TRANSGLUTAMINASE				

First Office Action

1.☑ Pursuant to the provision of Article 35 (1) of the Chinese Patent Law, the examiner made an examination as to substance of the captioned patent application for invention upon the request for substantive examination filed by the applicant on _____.

☐ Pursuant to the provision of Article 35 (2) of the Chinese Patent Law, the Chinese Patent Office has decided to conduct on its own initiative an examination as to substance of the captioned patent application for invention.

2.☑ The applicant requests taking the filing date, Jul. 4, 1997, at the JP Patent Office, the filing date, _____, at the _____ Patent Office, the filing date, _____, at the _____ Patent Office as the priority date of the present application.

☑ A copy of the first filed patent application certified by the receiving organ of the initial country of filing has been submitted by the applicant.

☐ A copy of the first filed patent application certified by the receiving organ of the initial country of filing has not been submitted by the applicant. Pursuant to the provision of Article 30 of the Chinese Patent Law, no priority right shall be deemed to have been claimed.

3.☑ The applicant filed amended application document(s) on Aug. 24, 1998 _____ and Apr. 14, 2000.

☐ Examination has confirmed that _____ filed on _____ cannot be accepted, _____ filed on _____ cannot be accepted,

as the above amendment(s) ☐ is/are not in conformity with the provision of Article 33 of the Chinese Patent Law.

☐ is/are not in conformity with the provision of Rule 51 of the Implementing Regulations of the Chinese Patent Law.

☐ For the specific reason that the amendment(s) cannot be accepted, see the text of

the Office Action.

4. ☐ The examination is conducted in the light of the original application document(s)
☑ The examination is conducted in the light of the following application document(s): in the original application documents submitted on the filing date: Claim(s) _____, page(s) 1-45 of the description, Figure(s) of the drawing(s); Claim(s) _____, page(s) _____ of the description, Figure(s) P. 1-7 submitted on Aug. 24, 1998; Claim(s) 1-29, page (s) _____ of the description, Figure(s) _____ submitted on Aug. 14, 2000
☐ Abstract of the description submitted on _____.

5. ☐ The present Office Action has been prepared without a search having been conducted.
☑ The present Office Action has been prepared with a search having been conducted.
☑ The following reference document(s) is/are cited in this Office Action (its/their serial number(s) will, continue to be used throughout the examination procedure):

filed with Application ←

No.	Number or Title of Document	Date of Publication (or filing date of interfering application)
1	EP 0481504 A1	(Date) Apr. 22, 1992 ,
2	Nature Vol. 326, P. 315	(Date) Mar. 19, 1987
3		(Date)
4		
5		
6		

6. The concluding comments of the examiner are:

☐ On the description:
☐ The content of the application comes within the scope where no patent right is granted as provided in Article 5 of the Patent Law.
☐ The description is not in conformity with the provision of Article 26(3) of the Patent Law.
☐ The drafting of the description is not in conformity with the provision of Rule 18 of the Implementing Regulations.
☑ On the claims:
☐ Claim comes within the scope where no patent right is granted as provided in Article 25 of the Patent Law.
☐ Claim is not in conformity with the definition of invention in Rule 2(1) of the Implementing Regulations.
☐ Claim _____ does not possess novelty as provided in Article 22(2) of the Patent Law.
☑ Claims 1-29 does not possess inventiveness as provided in Article 22(3) of the Patent Law.
☐ Claim _____ does not possess practical applicability as provided in Article 22(4) of

the Patent Law.

☑ Claims 1, 3, 10 are not in conformity with the provision of Article 26(4) of the Patent Law.

☐ Claim _____ is not in conformity with the provision of Article 31(1) of the Patent Law.

☐ Claim _____ is not in conformity with the provisions of Rules 20-23 of the Implementing Regulations.

☐ Claim _____ is not in conformity with the provision of Article 9 of the Patent Law.

☐ Claim _____ is not in conformity of the provision of Rule 12(1) of the Implementing Regulations.

For specific analyses of the above concluding comments, see the text of this Office Action.

7. In view of the above concluding comments, the examiner holds that:

☐ The applicant should amend the application document in accordance with the requirements raised in the text of this Office Action. The amended document(s) should be submitted in duplicate and should conform to the provisions of Article 33 of the Patent Law and Rule 51 of the Implementing Regulations of the Chinese Patent Law.

☑ The applicant should expound in his Observations the reasons why the captioned patent application is patentable and amend the places not conforming to regulations as pointed out in the text of the Office Action, otherwise it would be impossible for the patent right to be granted.

☐ The captioned patent application contains no substantive content for which the patent right may be granted, thus if the applicant has not advanced his reasons or has not done so adequately, the application will be rejected.

8. The applicant should pay attention to the following matters:

(1) In accordance with the provision of Article 37 of the Patent Law, the applicant should submit his/its Observations within **four** months from the date of receipt of this Office Action; if, without any justified reason, the time limit for making response is not met, the application will be deemed to have been withdrawn.

(2) The amendments made by the applicant to his application should conform to the provision of Article 33 of the Patent Law, the amended text should be in duplicate and the format should conform to the relevant provisions of the Guidelines for Examination.

(3) The applicant's Observations or amended text should be mailed or presented to the Receiving Section of the Chinese Patent Office. Document no mailed or presented to the Acceptance Section have no legal force.

(4) Without making an appointment, the applicant and/or agent may not come to the Chinese Patent Office to hold an interview with the examiner.

9. This Office Action consists of the text portion totalling 6 page(s) and of the following annex(es):

☑ 1 duplicate copies of the reference document(s) cited totalling 55 page(s).

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TEXT OF FIRST OFFICE ACTION

The present application relates to a process for producing microbial transglutaminase.

1. Claim 1 claims a protein having a transglutaminase activity, which comprises a sequence ranging from serine residue at the second position to proline residue at the 331st position in an amino acid sequence represented by SEQ ID No. 1 wherein the N-terminal amino acid of the protein corresponds to serine residue at the second position of SEQ ID No. 1. Reference document has disclosed a protein having a transglutaminase activity, whose sequence comprises 331 amino acids. Said protein differs from the 330 amino acids in claim 1 as shown in SEQ ID No. 1 merely in that the N-terminal of said protein bears an additional aspartic acid, i.e., the N-terminals of the recombinant protein being produced are Met-Asp-Ser and Met-Ser respectively. The efficiencies of methionine aminopeptidase for cleaving the N-terminal methionine of these two different proteins are different. When the recombinant protein has an N-terminal of Met-Ser, the efficiency of methionine cleavage is high; when the recombinant protein has an N-terminal of Met-Asp-Ser, the efficiency of methionine cleavage is low. Reference document 2 Nature Vol. 326, p315 (see Table 1 thereof) has disclosed that the cleavage efficiency of methionine aminopeptidase varies with the variation in the successive amino acid. When methionine is followed by alanine, glycine, proline, serine and threonine, methionine can be easily cleaved, and the residue at the

second position of such protein having a transglutaminase activity is exactly a serine. By combining reference documents 1 and 2, to obtain the protein having transglutaminase activity, which is deficient in aspartic acid, is easy to persons skilled in the art, i.e., on the basis of reference document 1, reference document 2 has given out definite technical hint to realize the object of improving the cleavage efficiency of methionine aminopeptidase. Moreover, their combination does not produce any unexpected effect. Hence, the technical solution claimed in claim 1 does not have prominent substantive feature and notable progress over reference documents 1 and 2, i.e. does not conform to the provision on inventiveness under Article 22(3) of the Chinese Patent Law.

For the same reason, claim 2 does not have prominent substantive feature and notable progress, i.e. does not conform to the provision on inventiveness under Article 22(3) of the Chinese Patent Law either.

2. Claim 3 claims a DNA which encodes for the protein of claim 1. Said DNA differs from that disclosed in reference document 1 (see Table 2 and page 3 in the description thereof) merely by some specific bases, which does not suffice to cause changes in encoding amino acid. Although the description of the present application has laid stress on the fact that codons change based on the affinity of Escherichia coli for codons, yet the bases of the DNA sequence in reference document 1 are also modified on the same principle. Moreover, there is no remarkable distinction between the two. Hence, the technical solution claimed in claim 3 does not have prominent substantive feature and

notable progress over reference document 1, i.e. does not conform to the provision on inventiveness under Article 22(3) of the Chinese Patent Law.

For the same reason, claims 4 to 11 do not have prominent substantive feature and notable progress, i.e. do not conform to the provision on inventiveness under Article 22(3) of the Chinese Patent Law either.

3. What is claimed in claim 12 is a recombinant DNA having a DNA of claim 3. Since the DNA of claim 3 does not have inventiveness, while recombination of DNA is the common technique in the art, claim 12 does not have prominent substantive feature and notable progress, i.e. does not conform to the provision on inventiveness under Article 22(3) of the Chinese Patent Law.

For the same reason, claims 13, 14 and 18 do not have prominent substantive feature and notable progress, i.e. do not conform to the provision on inventiveness under Article 22(3) of the Chinese Patent Law either.

4. The additional technical feature of claim 15 concerns: having a promoter selected from the group consisting of trp, tac, lac, trc, λ PL and T7. However, use of these promoters has been uncovered and well-known in the art. Hence, on the premise that the claim, which claim 15 refers to, does not have inventiveness, claim 15 does not have prominent substantive feature and notable progress, i.e. does not conform to the provision on inventiveness under Article 22(3) of the

Chinese Patent Law either.

For the same reason, claims 16 and 17 do not have prominent substantive feature and notable progress, i.e. do not conform to the provision on inventiveness under Article 22(3) of the Chinese Patent Law either.

5. The additional technical feature of claim 19 concerns that: transformation is conducted by use of a multi-copy vector. Reference document 1 (see page 13 in the description thereof) has disclosed the instance of using pUC19 as vector. Plasmid pUC19 belongs to multi-copy vector. Hence, on the premise that claim 19 refers to claim 18, claim 19 does not have prominent substantive feature and notable progress, i.e. does not conform to the provision on inventiveness under Article 22(3) of the Chinese Patent Law either.

   For the same reason, claims 20 and 21 do not have prominent substantive feature and notable progress, i.e. do not conform to the provision on inventiveness under Article 22(3) of the Chinese Patent Law either.

6. Claim 22 claims a process for producing a protein having a transglutaminase activity. Since the transformant participated therein does not have inventiveness, while the other technical features pertain to the common technical knowledge in the art, claim 22 does not have prominent substantive feature and notable progress, i.e. does not conform to the provision on inventiveness under Article 22(3) of the

Chinese Patent Law.

For the same reason, claims 23, 24 and 25 do not have prominent substantive feature and notable progress, i.e. do not conform to the provision on inventiveness under Article 22(3) of the Chinese Patent Law either.

7. Claim 26 claims a DNA which codes for a protein having transglutaminase activity and comprising an amino acid sequence represented by SEQ ID No. 1, wherein the base sequence coding for Arg at the fifth position from the N-terminal amino acid is CGT or CGC, and the base sequence coding for Val at the sixth position from the N-terminal amino acid is GTT or GTA. Reference document 1 has disclosed a protein having transglutaminase activity, whose sequence is totally identical to that as listed in SEQ ID No. 1; the coding DNA thereof, though showing variance with the degeneration of codons, is also designated on the basis of those codons which Escherichia coli manifests affinity for. Despite the minor variance between the two, they serve to solve the technical problem in the same approach, and the effects thereof show no remarkable distinction. Hence, claim 26 does not have prominent substantive feature and notable progress over reference document 1, i.e. does not conform to the provision on inventiveness under Article 22(3) of the Chinese Patent Law.

For the same reason, claims 27, 28 and 29 do not have prominent substantive feature and notable progress, i.e. do not conform to the provision on inventiveness under Article 22(3) of the Chinese Patent

Law either.

Even if the applicant can overcome the aforesaid problems of inventiveness, claims 1, 3 and 10 still are subject to the problem of lack of support from the description. Since all these claims relate, either directly (for claims 1 and 10) or indirectly (for claim 3), to the concept of "ranging from", based on these open-style claims, persons skilled in the art would not likely deduce that all the proteins comprising the sequence as represented by SEQ ID No. 1, besides those comprising the sequence as from 2nd to 331st position of SEQ ID No. 1, can serve to achieve the same object of invention. Hence, claims 1, 3 and 10 are not supported by the description, i.e. do not conform to Article 26(4) of the Chinese Patent Law.

For the aforesaid reasons, the independent claims and dependent claims of the present application do not have inventiveness. Moreover, the description does not have any other patentable substantive content. Hence, even if the applicant recombines the claims and/or further defines them on the basis of the content in the description, the present application still will not have the prospect of being granted the patent right. If the applicant fails to give adequate reasons to show that the present application has inventiveness over reference documents 1 and 2 within the time limit for making the response as prescribed in this Office Action, the present application shall be rejected.